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(S)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/434,870	11/04/99	HUSE	W P-IX-3458
<input type="checkbox"/>		HM12/1023	<input type="checkbox"/> EXAMINER HELMS, L
			<input type="checkbox"/> ART UNIT 1642
			<input type="checkbox"/> PAPER NUMBER 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/434,870	HUSE ET AL.
	Examiner Larry R. Helms	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 August 2001.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 42-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 42-51 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8</u>	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

1. Claims 1-41 have been canceled.
Claims 42-51 have been added.
2. Claims 42-51 are under examination.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action
4. The following Office Action contains some NEW GROUNDS of rejection necessitated by amendment.

Response to Arguments

5. The rejection of newly submitted claims 42-51 under 35 USC 112 first paragraph is maintained and ~~made~~^{made} again.

The response filed 8/20/01 has been carefully considered but is deemed not to be persuasive. The response states "applicants respectfully submit that the instant claims (i.e. claims 42-51) are fully enabled". In response to this argument, the newly submitted claims encompass mixing oligonucleotides in any order and under conditions that allow for hybridization to create overlapping oligos (see step (c) in claims 42 and 47). The claims encompass oligos that code for only framework regions or only CDRs and oligos that encode CDRs in any order. The specification fails to teach heavy or light chains wherein the CDRs are in any random order. The method is for the construction of a heavy or light chain variable region which by definition comprises CDRs and framework regions. The specification does not teach a heavy or light chain

variable region or only CDRs or only frameworks. Thus, as previously discussed the art of Rudikoff et al clearly teaches a heavy chain and a light chain comprises CDRs and frameworks in the correct order.

The following are some NEW GROUNDS of rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 42-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 42 and 47 have been amended to recite the phrase "three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia". The response of 8/20/01 states that "applicants respectively submit that, should that particular residue fall into the definition of a CDR residue by either the Kabat or Chothia definition, then that residue is properly considered to be a CDR residue" See page 10 of response). This is not persuasive because the response does not state where support for the phrase can be found in the application as originally filed. The specification discloses the definitions of both Kabat and Chothia separately (see page

8) but the specification does not disclose "a combined definition". Applicants are required to either point to specific support for the phrase in the original application or remove it from the claims.

8. Claims 42-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 42 and 47 recites the limitation "first reference nucleic acid sequence" in claims 42 and 47. There is insufficient antecedent basis for this limitation in the claim.

b. Claims 42-51 are indefinite for reciting the term "portion" because the exact meaning of the term is not clear. Does the term mean an amino acid when directed to proteins or a nucleotide when directed to DNA?

Claim Rejections - 35 USC § 103

9. Claims 42-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deng et al (Canadian Patent 2,125,240 A1, published 12/7/95, IDS #8)

The claims recite a method of constructing a heavy or light chain variable region encoding nucleic acids comprising providing a donor sequence and an acceptor sequence and chemically synthesizing a population of oligos encoding for at least one modified CDR wherein at least one amino acid is different from the reference sequence and a second population of oligos encoding modified framework regions wherein one or

more amino acids are changed compared to the reference sequence and mixing and constructing the nucleic acids. Further co expressing the population with a light or heavy chain and wherein the acceptor is human.

Deng et al teach a method of producing a population of heavy or light chains wherein the CDRs are randomized and the framework regions are randomized (see page 12, lines 28-32, 13, lines 4-6, 12-14, Figure 2, page 22-23). The method comprises chemical synthesis of oligos and framework regions are randomized wherein the residues randomized are those that differ between the murine and the human (see page 22-23) and mixing oligos to construct the nucleic acid library. Deng does not specifically teach that the reference sequences are in electronic form.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have the first and second reference sequences to be in electronic form.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have the first and second reference sequences to be in electronic form because it is customary at the time the claimed invention was made to have computer databases with antibody sequences of both mouse and human such as the NEW sequence in Cheng et al (see page 35, line 37).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

10. No claim is allowed.
11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Art Unit: 1642

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Sheela J Huff
SHEELA HUFF
PRIMARY EXAMINER